ABSTRACT

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Title of Thesis: Preparation of phenylcarbamoylpyrazine-2-carboxylic acid derivatives as potential antitubercular drugs

Tuberculosis still represents a major public health issue all over the world. The increasing number of newly detected multi-drug resistance cases indicates that there is an urgent need of discovery of new antituberculotics addressed towards new and specific targets. This is accompanied by the development of new and effective synthetic methods.

This work provides an introduction to tuberculosis and its treatment. Furthermore it covers a microwave-assisted synthesis of organic acid esters and synthesis of pyrazinamide derivatives as potential antituberculotics whereas pyrazinamide is one of the most used antitubercular drugs nowadays. Series of substituted 3-(phenylcarbamoyl)pyrazine-2-carboxylic acid derivatives and their methyl esters were synthesized. Final products were characterized by ^{1}H and ^{13}C NMR and IR spectroscopy, elementary analysis was performed and melting point was measured. Lipophilic parameters log *P* and Clog *P* were calculated and log *k* was measured experimentally. Antimycobacterial, antifungal and antibacterial activity of newly prepared compounds were tested. The three phenylcarbamoyl acids with R = 4-Br, R = 2-OH and R = 4-$N(CH_3)_2$ substitution exerted moderate antimycobacterial activity with MIC 50 $\mu g.ml^{-1}$ against *Mycobacterium tuberculosis* $H37R_v$. Structural modifications that could lead to more effective derivatives were discussed.